

- a) a purified first moiety containing a first antigen binding region bound to a first antigen non-binding region via a peptide linker; and
- b) a purified second moiety containing a second antigen-binding region bound to a second antigen-non-binding region via a peptide linker, whereby the moieties are engineered so as to be juxtaposed to each other in [an unnatural] a counterpoised configuration, [and] wherein the first moiety and second moiety are derived from the same gene, and wherein the first moiety and the second moiety are light chain variable domains.

Please add the following new claims.

- 22. The molecule as recited in claim 10, wherein the peptide linker joins the C-terminus of one variable light chain domain to the N-terminus of a second variable light chain domain.
- 23. The molecule as recited in claim 10, wherein the molecule is a Janusbody construct.
- 24. The molecule as recited in claim 10, wherein the molecule is a dimer of variable light chains selected from the group consisting of Len, Rec, Jto, Wil, Loc, Wat, Cle, Rhe, and combinations thereof.
- 25. The molecule as recited in claim 10, wherein the counterpoised configuration of the first and second moieties is the result of amino acid substitutions at specific sites.
- 26. The molecule as recited in claim 24, wherein the counterpoised configuration of the first and second moieties is due to excess negative charge at the modified site.
- 27. The molecule as recited in claim 24, wherein the amino acid substitution is replacement of glutamine 38 with glutamic acid.
- 28. The molecule as recited in claim 24, wherein the amino acid substitution is replacement of lysine 30 with threonine.
- 29. The molecule as recited in claim 24, wherein the dimer formation is achieved by mutations selected from the group of amino acid substitutions comprising substituting lysine 30 with threonine, glutamine 89 with alanine, glutamine 89 with leucine, glutamine

38 with glutamic acid, and combinations thereof.

30. The molecule as recited in claim 27, wherein the two moieties have an association constant of approximately  $5.8 \times 10^5 \text{ M}^{-1}$ .

31. The molecule as recited in claim 28, wherein the two moieties have an association constant of approximately  $0.8 \times 10^5 \text{ M}^{-1}$ .

32. An isolated molecule consisting of two light chain variable domains, the said light chain variable domains being modified light chain variable domains from immunoglobulin molecules, wherein the said modification is replacement of an acidic amino acid with a hydrophobic amino acid.

33. The molecule as recited in claim 32, wherein the light chain variable domains are immunoglobulin molecules selected from the group consisting of Len, Rec, Jto, Wil, Loc, Wat, Cle, Rhe, and combinations thereof.

34. The molecule as recited in claim 32, wherein the modification is replacement of glutamine 89 with alanine.

35. The molecule as recited in claim 32, wherein the modification is replacement of glutamine 89 with leucine.

36. The molecule as recited in claim 32, wherein the addition of the hydrophobic amino acid results in two to three orders of magnitude increased affinity between the dimer subunits, compared to the affinity between natural dimer subunits.

37. The molecule as recited in claim 34, wherein the two variable light chains have an association constant approximately greater than  $10^8 \text{ M}^{-1}$ .

38. The molecule as recited in claim 35, wherein the two variable light chains have an association constant of approximately  $4 \times 10^6 \text{ M}^{-1}$ .

### REMARKS

#### Informalities

The Examiner requests a proper information disclosure statement under 37 CFR 1.98(b). The Applicants respectfully submit such a statement, herewith.

The drawing in the application is objected to by the Draftsperson under 37 CFR 1.84, per the Notice of Draftsperson's Review (Form PTO 948), dated November 9, 1999.